

INTERNATIONAL APPLICATION PUBLISHED UNDER 'THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:

A61K 47/48, 35/14, 35/12, 31/57, 31/365, 38/13, 39/05 // C07K 16/28

(11) International Publication Number:

WO 96/32137

(43) International Publication Date:

17 October 1996 (17.10.96)

(21) International Application Number:

PCT/US96/05087

(22) International Filing Date:

12 April 1996 (12.04.96)

(30) Priority Data:

US

Filed on

08/422,100 60/088,104

(60) Parent Applications or Grants

(63) Related by Continuation

14 April 1995 (14.04.95)

US 30 October 1995 (30.10.95) US (72) Inventors; and

(75) Inventors/Applicants (for US only): NEVILLE, David, A. [US/US]; 9624 Parkwood Drive, Bethesda, MD 20814 (US). SCHARFF, Joshua, E. [US/US]; 4600 Harlan Street, Rockville, MD 20853 (US). THOMAS, Judith [US/US]; 2117 Brook Highland Ridge, Birmingham, AL 35242 (US).

(71)(72) Applicant and Inventor: KNECHTLE, Stuart, J. [US/US];

2268 Caine Road, Oregon, WI 53575 (US).

(74) Agents: NEEDLE, William, H. et al.; Needle & Rosenberg, Suite 1200, 127 Peachtree Street, N.E., Atlanta, GA 30303-1811 (US).

14 April 1995 (14.04.95) 60/088,104 (CIP)

08/422,100 (CIP)

US 30 October 1995 (30.10.95) Filed on

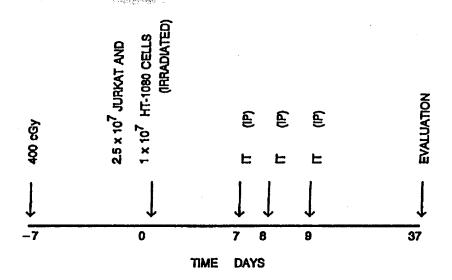
(71) Applicants (for all designated States except US): THE GOV-ERNMENT OF THE UNITED STATES OF AMERICA, represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; National Institutes of Health, Office of Technology Transfer, Box OTT, Bethesda, MD 20892-9902 (US). UNIVERSITY OF ALABAMA RESEARCH FOUNDATION [US/US]; Suite 1120-G, 701 South 20th Street, Birmingham, AL 35294-0111 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published

Without international search report and to be republished upon receipt of that report.

(54) Title: METHODS OF INDUCING IMMUNE TOLERANCE USING IMMUNOTOXINS



(57) Abstract

ಶ

¢

Provided is a method of treating an immune system disorder not involving T-cell proliferation, comprising administering to the animal an immunotoxin comprising a mutant diphtheria toxin moiety linked to an antibody moiety which routes by the anti-CD3 pathway, or derivatives thereof under conditions such that the disorder is treated. Thus, the present method can treat graft-versus-host disease. Also provided is a method of inhibiting a rejection response by inducing immune tolerance in a recipient to a foreign mammalian donor tissue or cells, comprising the steps of: a) exposing the recipient to an immunotoxin so as to reduce the recipients' peripheral blood T-cell lymphocyte population by at least 80 %, wherein the immunotoxin is anti-CD3 antibody linked to a diphtheria protein toxin, wherein the protein has a binding site mutation; and b) transplanting the donor cells into the recipient, whereby a rejection response by the recipient to the donor organ cell is inhibited, and the host is tolerized to the donor cell.